MEDICAL PROCEEDINGS

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IN THIS ISSUE · IN HIERDIE UITGAWE

MEDICAL OFFICER FOR ENTOKOZWENI WELFARE CENTRE

A medical officer is required for this Centre at Alexandra Township, Johannesburg, for one 3-hourly session per week. Salary: £2.10.0 per session inclusive of transport.

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Medical Proceedings · Mediese Bydraes

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Pfizer

INTERNATIONAL

medical news bulletin

Current Developments in the Fields of Antibiotics, Hormones, Nutrition and Clinical Medicine

Prepared for Physicians by the Medical Department of Pfizer International, Inc., 25 Broad Street, New York 4, N.Y., U.S.A

Vol. 111, No. 11, 1956

TWO NEW PFIZER ANTIBIOTICS !

SIGMAMYCIN*: IMPORTANT NEW ANTIMICROBIAL AGENT - Pfizer, discoverer of the outstanding broad-spectrum antibiotic, tetracycline, continues to pioneer in the development of life-saving antibiotics. Pfizer teams of scientists identified a new exceptionally well-tolerated antimicrobial agent (oleandomycin**) which, combined with tetracycline, solves the problem of resistance created by continued use of the tetracyclines. The name of the new combined antibiotic is SIGMAMYCIN. It combats many strains of staphylococci and other pathogens now resistant to broad-spectrum therapy. It also helps prevent the emergence of new resistant strains. Extensive tests indicate that it shows a most marked degree of synergism. In studies conducted by English et al.[1] with microorganisms of varied source including 21 antibiotic-resistant varieties of M. pyogenes var. aureus, the minimum inhibitory concentration of Sigmamycin was less than that of either component used independently. They found, furthermore, that the combined antibiotic "gives significantly greater protection than could be expected from the additive effects of the two drugs given separately at appropriate dosage levels." No antagonism was observed in any of their studies.

Studies with Sigmamycin indicate that it provides enhanced activity, is unusually well tolerated, and should prove particularly useful for the great majority of patients requiring broad-spectrum therapy when sensitivity-testing is not practical. - NOTE:- Sigmamycin is being currently evaluated in many countries including South Africa and will become available to the medical profession during early 1957.

MATROMYCIN: REMARKABLY EFFECTIVE AGAINST STAPHYLOCOCCI - Matromycin, brand of oleandomycin, discovered by Pfizer in 1954, is highly useful by itself in situations in which broad-spectrum therapy is not required, but where resistance is a factor in infection of known bacterial (especially staphylococcal) origin. Oleandomycin is clinically an exceptionally safe, well-tolerated drug. Marmell and Prigot[2] have used oleandomycin to treat 3 patients with donovanosis. All responded "favorably"; lesions healed after 25-75 Gm. dosage. No side effects.

*Combination of oleandomycin and tetracycline

**Available from Pfizer as Matromycin (Trademark)

COMBINED ANTIBIOTIC THERAPY RECOMMENDED FOR STREPTOCOCCAL ENDOCARDITIS, says Hamburger.[3] This regimen, he believes "takes advantage of the synergistic action of penicillin and streptomycin and is best for endocarditis caused by penicillin-sensitive streptococci." The recommended dose is 600,000 U. of procaine penicillin q. 6 h. intramuscularly and 1 Gm. of a combination of streptomycin and dihydrostreptomycin q. 12 h. intramuscularly for 2 weeks. "On this regimen the temperature usually falls to normal within the first 48 hours and the patient soon begins to feel better."

TERRA-CORTRIL®* "MOST BENEFICIAL" IN DERMATOSES - Oxytetracycline-hydrocortisone ointment can be expected to evoke the "most beneficial results" in skin disorders complicated by secondary bacterial infection, say Welsh and Ede.[4] Combining the antibiotic with hydrocortisone offers the advantage that Terramycin combats infection while hydrocortisone controls the underlying disorder through its anti-inflammatory action. After treating 232 patients with various skin disorders (170 with secondary and 62 with primary bacterial infection), authors recommend that the ointment be applied to the affected areas t.i.d. and the patients be examined at weekly intervals. Although in many cases treatment was given for only a week, therapy had to be continued in some patients for several months to control eczematization or prevent recurrence of infection in denuded areas. Over-all therapeutic response was "excellent" in 184 and "fair" in 47 patients.

In another report, Downing and Folan[5] emphasize that in 48 patients with various dermatoses, hydrocortisone had the primary effect on the disease. Terramycin may have prevented, in some patients, and eradicated in others, the secondary infection already present and thus speeded the response to hydrocortisone. In 5 patients with primary pyogenic dermatoses, Terramycin, however, was chiefly responsible for the good result obtained.

AKLAVIN, NEW ANTIPHAGE - Strelitz and colleagues[6] report the isolation of crystalline, orange-colored salts of a new antibiotic, named aklavin, active against bacterial viruses. The substance seems to consist of mixtures of several closely related chemical individuals. Crude lyophilized hydrochloride of aklavin gave zones of complete inhibition for phages of B. megaterium, Escherichia coli T-2 and T-5, paratyphoid A, and cholera phages C, D, E, H, J, M, and R. It also inhibited the Y-SK poliomyelitis virus in tissue culture. Aklavin, say the authors, appears to affect the host-parasite relationship rather than to have a phagocytic action. A much higher concentration was needed to inactivate free phage particles than to prevent lysis in the serial dilution tests.

MENINGITIS SHOWS "GOOD CLINICAL RESPONSE" TO ANTIBIOTICS - Two cases of meningitis following lumbar puncture - a rare complication - are reported by Majka, Gysin and Zaayer.[7] Symptoms included extreme headache, nausea, vomiting, and twitching of the musculature. Both patients received combined antibiotic therapy (penicillin, streptomycin) and sulfadiazine for 7 days, together with hydration therapy. "Recovery was complete and uneventful.... No residuals of the meningitis were noted."

ANTIBIOTICS AROUND THE WORLD

AUSTRIA: TERRAMYCIN "DRUG OF CHOICE" IN CAT SCRATCH DISEASE - Four patients with virus scratch lymphadenitis were "cured" in a "relatively short time" with Terramycin. Schmid[8] notes the difficulties in differential diagnosis between this disease, tuberculosis, tularemia, and lymphogranuloma inguinale. Therapy, aside from surgical intervention, "consists above all in administration of antibiotics, among which Terramycin is the drug of choice."

*Pfizer brand of oxytetracycline combined with hydrocortisone

GREECE: TERRAMYCIN "SPECTACULAR" IN PERITONITIS - "...Terramycin is a particularly effective antibiotic" in peritonitis and gives better results than penicillin and streptomycin, says Mouzas.[9] Of 24 patients, 11 received 1 Gm. intravenous Terramycin a day, for 5 days, and the rest a penicillin-streptomycin combination. "Really spectacular results" were obtained with Terramycin: hyperthermia disappeared in 4 days; hospitalization did not exceed 4 weeks. The streptomycin-penicillin combination showed "incontestably less brilliant, although nevertheless satisfactory, results."

MEXICO: WHOOPING COUGH AND TERRAMYCIN INTRAMUSCULAR - "A great variety of infectious diseases of the upper and lower respiratory tracts has been effectively overcome by the administration of intramuscular Terramycin." In whooping cough, says Sauza,[10] the antibiotic given intramuscularly is of "special value" when gastrointestinal symptoms prevent oral administration. Also, in infants and young children Terramycin Intramuscular assures exact dosage and adherence to a prescribed regimen.

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HORMONES

HYDROCORTISONE HELPED CONTROL THROMBOCYTOPENIA which developed in a patient after transfusion with bank blood. The hormone was given in doses of 300 mg./day for 8 days, then reduced to 75 mg./day; the decreased dose was continued even after the patient was discharged from hospital, until she had gained 20 lb. The steroid "helped control the bleeding," Kaetz and colleagues[1] conclude. Bleeding began to ebb 4 days after start of therapy and long before platelet count rose to even near-normal levels.

HYDROCORTISONE "DRUG OF CHOICE" IN SHOCK - "...the effectiveness of intravenous hydrocortisone was fully as great as expected" in 30 surgical patients, say Ehlers and Heinzel.[2] Indications were postoperative shock, shock prophylaxis in geriatric surgery, prophylaxis of acute adrenal insufficiency, shock and collapse after severe accidents, and severe burns. "The effectiveness of intravenous hydrocortisone is very rapid; it therefore is often the drug of choice in states of shock and collapse caused by adrenal insufficiency." Dosage: one or more 100 mg. i.v. injections of hydrocortisone.

STEROIDS AND BACTERIOSTASIS - In vitro studies with prednisolone and prednisone revealed "that they did not interfere with the inhibitory effect of bacteriostatic antibiotics, namely the broad spectrum group...and combination of streptomycin plus broad spectrum group," say Seneca and colleagues.[3] They also found that addition of prednisolone to tetracycline gave complete protection in Streptococcus pyogenes infections of mice. Dosage: 0.01 mg. prednisolone plus 2 mg. tetracycline in repeated doses given intraperitoneally every day for 5 days.

REPORT FROM ITALY: PREDNISOLONE IN VARIOUS DISEASES

DIABETES INSIPIDUS - "Immediate and surprising" results were achieved with prednisolone in one patient suffering from diabetes insipidus. Lucherini[4] reports that within 24 hours, polydipsia and polyuria ceased and were maintained at a normal level even after treatment was discontinued.

RHEUMATOID ARTHRITIS - "Favorable results were obtained with prednisolone in 32 patients suffering from rheumatoid arthritis," observe Lucherini and colleagues.[5] The steroid, say the authors, "represents an undeniable progress" in antirheumatic treatment.

DERMATOLOGY - The effectiveness of prednisolone in dermatologic infections is especially seen in pemphigus vulgaris, says Zuccarini.[6] Without harmful influence on metabolic functions, the steroid has a "favorable" effect on other dermatologic diseases. Cannata[7] also obtained "consistently brilliant therapeutic results" with prednisolone in a wide variety of dermatologic disorders. [See note 1 below]

PREDNISONE, "POTENT WEAPON" IN TREATMENT OF ALLERGIC DISORDERS - Prednisone was "highly effective in the temporary symptomatic relief of asthma and atopic eczema" in 16 children, 7 months to 11 years old. Siegel and colleagues[8] note that although somewhat dependent on age, weight, and severity of disease, the needed dosage was relatively high as compared to that in adults. A suppressive dose of 20 mg. seemed adequate for most of the older children; maintenance dose varied from 5 mg. in a one-year-old and up to 15 mg. in older children. "There can be no doubt that prednisone is an extremely potent weapon in the treatment of allergic disorders of children as well as of adults."

GERMANY: CORTRIL® PRAISED FOR RELIABILITY IN ECZEMA - Zeisel and colleagues[9] find Cortril Topical Ointment "simple" to use and "reliable" in its effect on eczema. "Success, evidenced by regression of inflammatory manifestations and of pruritus," was observed after one to two days, in 35 patients with various forms of eczema. The "inflammation-inhibiting action of the topically administered and percutaneously effective hydrocortisone" and its effectiveness after a short period of administration are praised. The 2.5% ointment was found "superior" to the 1%. [See note 2 below]

NOTE 1: Prednisolone supplied by Pfizer as Deltacortil,® white, scored, 5 mg. tablets, bottles of 10, 20 and 100; in the familiar Pfizer oval shape.

NOTE 2: Cortril (brand of hydrocortisone free alcohol) Topical Ointment, 1.0% (10 mg.) available in 1/6 oz. tubes; 2.5% (25 mg.), in 1/6 oz. tubes.

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REDAKSIONEEL · EDITORIAL

WETSONTWERP OP AANVULLENDE GESONDHEIDSDIENSTE

Die Gekose Komitee oor die onderwerp van die Wetsontwerp op Aanvullende Gesondheidsdienste wat op 16 Januarie 1956 op las van die Volksraad opnuut aangestel is, het oorweging verleen aan die onderwerp van die wetsontwerp, asook aan die getuienis en memorandums wat tydens die 1956-sessie en gedurende die voorafgaande sittings van die Parlement aan hom voorgelê is.

Die Gekose Komitee het tot die gevolgtrekking geraak dat dit in die huidige omstandighede onprakties sou wees om wetgewende voorsiening in 'n enkele wetsontwerp te maak vir al die uiteenlopende belange van die verskillende groepe wat aanvullende gesondheidswerk doen.

Die Gekose Komitee het gevolglik aanbeveel dat daar nie voortgegaan moet word met die Wetsontwerp op Aanvullende Gesondheidsdienste nie. Met die oog op die feit dat daar geen dringende behoefte is aan wetgewing in verband met hierdie saak nie, lyk dit asof dit hoogs wenslik sou wees dat aanvullende gesondheidsdienste moet voortgaan om te funksioneer op die grondslag wat reeds deur gewoonte en tradisie neergelê is.

Dit skyn asof dit nie veel nut sal hê nie en trouens heelwat gevaar kan meebring as die posisie van heeltemal onbelangrike ondernemings verheerlik word deur 'n statutêre status aan hulle te verleen.

DOKTERS EN TOEBEREIDINGSWERK

Daar is rede om aan te neem dat 'n nuwe aanval tydens die eersvolgende sitting van die Parlement gedoen sal word op die statutêre en tradisionele reg van mediese praktisyns om hul eie preskripsies toe te berei.

Hierdie poging om afbreuk te doen aan die professionele voorregte en pligte van die dokter, veral op die platteland, kan nie geregverdig word òf op morele òf op ekonomiese gronde nie; en (uit die standpunt van die pasiënt) kan dit bes moontlik aanleiding gee tot 'n onnodige, onwenslike en voorkombare verhoging van die koste wat deur siekte en die ondersoek daarvan meegebring word.

Sekere kleinhandelsaptekers dring reeds aan op 'n groter winsmarge t.o.v. die ‚etiese' produkte wat deur hulle verkoop word. Hulle is nie tevrede met 'n wins van een-derde op die prys wat die pasiënt betaal nie (d.w.s. 50% op die kosprys), maar verlang dat dit verhoog moet word tot 40% van die prys wat die verbruiker betaal (d.w.s. ongeveer 66% op die kosprys), uitsluitende die sogenaamde toebereidingsgeld.

Ons verdedig nie die mediese praktisyn wat onbillike handel dryf vir sover dit toebereidingswerk betref nie, veral as hy meeding met die kleinhandelsapteker in stryd met die Geneeskundige Raad se etiese beslissing oor hierdie saak.

Wat egter skynbaar nodig is, is nie 'n beperking van die toebereidingsreg van die geneesheer nie, maar 'n ondersoek na die prys wat die pasiënt moet betaal vir die middels wat vir hom voorgeskryf word—afgesien van wie daardie middels verskaf.

SUPPLEMENTARY HEALTH SERVICES BILL

The Select Committee on the subject of the *Supplementary Health Services Bill*, which was reappointed by Order of the House of Assembly on 16 January 1956, considered the subject matter of this Bill, together with the evidence and memoranda submitted to it by interested bodies during the 1956 session and during previous sessions of Parliament.

The Select Committee concluded that it would be impracticable, in the present circumstances, to make legislative provision in one Bill which would adequately serve the divergent interests of the various groups performing supplementary health services.

The Select Committee accordingly recommended that the *Supplementary Health Services Bill* be not proceeded with. In view of the fact that there can be no urgency for legislation in connexion with this matter, it would seem highly desirable that supplementary health services should continue to function along the lines determined by custom and tradition.

There seems little point and much danger in aggrandizing the position of quite minor undertakings by enhancing them with a statutory status.

DOCTORS AND DISPENSING

There is reason to believe that a new assault will be made (during the next session of Parliament) upon the statutory and traditional right of medical practitioners to dispense their own prescriptions.

This attempt to diminish the professional privileges and duties of the doctor, especially in rural areas, cannot be justified either on moral or on economic grounds; and (from the standpoint of the patient) may well lead to an unnecessary, undesirable and preventable increase in the cost of illness and its investigation.

Certain retail pharmacists are already pressing for a greater profit margin on 'ethical' preparations. They are not satisfied with a profit of one third of the cost to the patient (i.e. 50% on cost) but want this raised to 40% of the price to the consumer (i.e. about 66% on cost), exclusive of a so-called dispensing fee.

We hold no brief for medical practitioners who trade improperly in dispensing, especially in competition with retail pharmacists, and in contravention of the Medical Council's ethical ruling on this matter.

What seems necessary, however, is not a restriction on the dispensing rights of the doctor, but an inquiry into the cost to the patient of the drugs prescribed for him, no matter who supplies them.

SKIN WOUNDS AND SURGICAL INCISIONS

THEIR EFFECTIVE CLOSURE WITH ADHESIVE TAPE

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and

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In previous studies[1, 2] attention was drawn to some aspects of the histogenesis of repair of surgical incisions which seem, hitherto, to have escaped the attention of histologists and pathologists. Among our findings, the following are of particular importance for the present communication:

1. Incisions are bridged first by epidermis and only later by connective tissue.

2. In wounds penetrating to certain depths (no matter how small their area) regenerating epidermis invariably 'invades' the underlying connective tissue during the early stages of repair (6th-16th post-operative days).

3. The repair of the dermal connective tissue seems to be stimulated, at least in part, by this 'invasive' tendency of regenerating epidermal cells. Consequently, connective tissue repair follows, by some days, the initial epithelial bridging of the incisional gap. In Man, connective tissue repair is well under way only after the 5th post-operative day.

Because our previous studies were conducted on serial sections, it was possible to investigate not only the healing of the incisions themselves (in experimentally inflicted wounds in animals and in Man), but also to analyse epidermal and dermal reactions to sutures and the genesis of suture needle puncture wounds. It was found that, as in the incisions, so too at the sites of suture needle puncture wounds in the skin, epidermis invades vigorously along the sutures, and especially along their outer aspect (relative to the incision). The epidermal and the connective tissue reactions to sutures (of various types) were frequently, if not invariably, more vigorous than those at the incision (Fig. 1). The reactions to the sutures, and at the suture needle puncture wounds in the epidermis, can seriously complicate healing, resulting in delayed union, suture cysts (with or without infections, Fig. 2), and the resulting scars may consequently be far from ideal, especially for plastic surgery, which aims at achieving cosmetically satisfying effects as a desirable, if not, in fact, as a basically essential end result.

In view of the foregoing findings, it was considered necessary to do a perhaps long overdue re-investigation of methods generally used for closing surgical skin incisions. Investigations were immediately started with a view:

i. To understand more fully the histogenesis of healing; and

ii. To improve the rate of healing and the scars ultimately resulting from surgical incisions.

Bearing in mind the findings (as briefly outlined) about the reactions to sutures, we aimed, if possible, to eliminate the use of sutures in the closure of the skin portion of surgical incisions. Our objectives were clear in principle, viz. that it was desirable:

A. To eliminate the puncturing of the epidermis by sutures, thereby preventing the complication of epidermal invasions and the dermal reactions both

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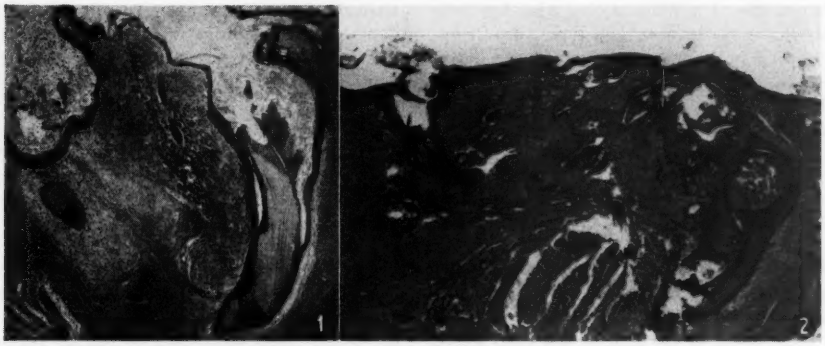

Fig. 1. Reactions are well shown to the incision (at left) and to the 6—0 suture and to the suture needle puncture wound (at right) at the 15th post-operative day in a rabbit. Note:
(*a*) Active invasion of dermis by epithelium both in the healing incision and around the suture.
(*b*) The vigorous connective tissue reaction to the suture and the lining of the suture track by epithelium. (× 25).

Fig. 2. At top left the healing incision and at right an epithelial-lined cyst formed around a 6—0 suture at the fifteenth post-operative day in a rabbit (× 43).

to the sutures and to their associated epidermal invasions.

B. If possible, to eliminate all sutures through or near the skin, since by so doing time could be saved and costs would be less—both in terms of the suturing material and especially in terms of the time of skilled personnel required for inserting and removing the sutures.

Moreover, the varying amounts of pain which are unavoidably inflicted by suturing and by post-operative removal of the sutures would also be eliminated.

Besides, no matter how carefully wounds are sutured, it has been our experience that it is virtually impossible, with suture closure, to obtain absolute linear apposition of the cut edges or to avoid *microscopically* detectable inversion of the epidermis into the incision.

A careful analysis of the literature revealed 3 important departures from the more generally adopted techniques of suturing incisions. These were:

1. Subcuticular stitching. This eliminates puncturing the epidermis by sutures and needles, but is time-consuming and therefore not suitable for general surgery. Besides, accurate co-aption of cut edges is difficult to achieve with this method.

2. The method[3] of opposing skin edges by suturing together plaster strips placed parallel with the edges of the incision. This method is of special value in children, but the stitching still required is time consuming and the opaque plaster does not permit visualization of the final apposition of the wound edges. It is also clumsier than ordinary suturing methods.

3. Finally, there is the seemingly ideal method of closing wounds by the use of clots, produced artificially, in plasma poured on to the incision, by the addition of calcium salts or of bovine thrombin. The method,[4] initially introduced for 'nerve suture' has been applied, with minor modifications, by several investigators to the closure of surgical incisions and for the application of free skin grafts.[4-6]

The results with these methods are generally described as excellent. However, in our hands, this method, while providing excellent results (when it works), is finicky, tends to be erratic, and demands special facilities and services for the provision of suitably collected reasonably fresh plasma, thrombin and calcium solutions. Besides, the edges of the wound are not adequately supported and, therefore, when such plasma closures of large wounds are effected, the surgeon is left feeling somewhat apprehensive of the possible rupture of wounds during the early post-operative period, especially during the unavoidable and almost invariable restlessness of patients recovering from general anaesthetics. Consequently, while plasma 'clot suture' of wounds would seem to be the most satisfactory and 'physiological', it has distinctly undesirable features and, besides, it is extremely expensive and almost if not quite as time consuming as ordinary suturing.

While experimenting with modifications of Radcliffe's method[3] for 'sutureless' wound closure, we read a report in the lay press that Willliamson of Colorado, U.S.A., had devised an adhesive tape for closing wounds. We

wrote to Dr. P. Williamson, who has very kindly made available several types of adhesive plastic tape with an adhesive made specifically for surgical purposes.

The following is a brief report of our initial findings with the experimental use of adhesive tape for closing surgical incisions in human volunteers.

MATERIAL AND METHODS

Duplicate sets of 2 or 3 incisions, 1½-3 inches long (i.e. 4 or 6 incisions in all, in each subject), extending down to subcutaneous fat (Fig. 3A), were made in the skin of the volar aspect of the forearms of 5 volunteers, under local anaesthesia (2% procaine) injected with a dental carpule syringe and a fine needle. Care was taken to avoid cutting large superficial veins. The directions of all the incisions were the same in each volunteer, but differed from subject to subject. *Longitudinal* incisions were purposely made in 2 subjects, to provide scars under the greatest tension in the forearm (Figs. 4, 5). Transverse incisions were made in the remaining 3 subjects (Fig. 3 A-D). In all cases, one or more incisions were inflicted through linear abrasions, made with a wire brush, rotated by a miniature DeSouttar compressed air tool which revolves at speeds up to 70,000 r.p.m. (according to the air pressure) —a method virtually identical with that des-

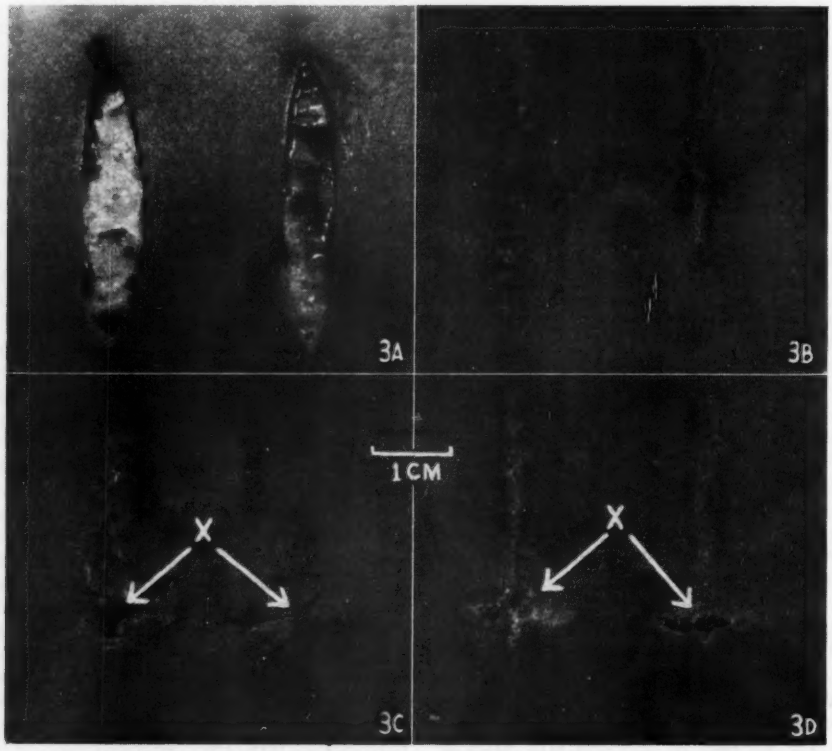

Fig. 3*A*. Appearance of skin incisions before closure.
Fig. 3*B*. At left, sutured wound; at right tape-closed wound at tenth post-operative day. Note erythema and oedema of wound edges in sutured wound and hair-line closure of taped wound.
Fig. 3*C*. Same wounds at sixteenth post-operative day when tape was removed from 10-day (transverse) biopsy wounds (X). Note excessive pigmentation and scaling around sutured wound and absence of these from taped wound (at right). Wrinkling of skin due to dressing.
Fig. 3*D*. Wounds at 26 days. Note hyperpigmentation and suture scars around sutured wound (reader's left), very fine scar of taped wound (right) and 'spreading' of 10-day taped biopsy wounds (X) from which tape was removed prematurely. Original taped incision was kept taped for 10 days and has *not* spread.

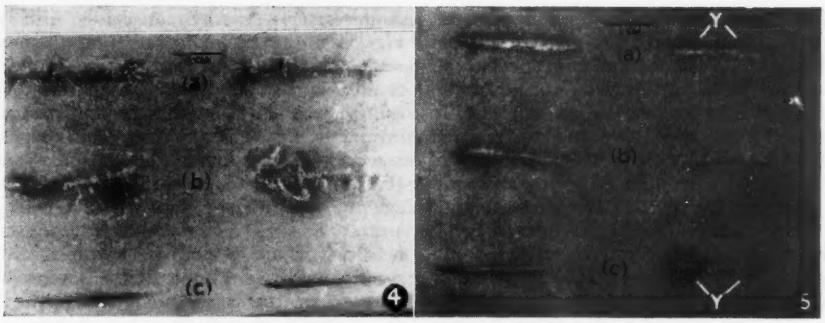

Fig. 4. (*a*) Sutured, show erythema and scaling.
(*b*) Abraded prophylactically and sutured.
(*c*) Taped only.
Tenth post-operative day; longitudinal incisions.

Fig. 5. Same wounds in same order (*a*, *b*, *c*) as in Fig. 4, but at 60 days post-operatively showing:
(i) Healing of original longitudinal and of 4 transverse tape-closed biopsy wounds (Y);
(ii That longitudinal scars are more marked than transverse biopsy scars (Y);
(iii) Scar of sutured wound (a) is more hypertrophic than that of taped wound (c).

cribed by Kurtin[8] and by Blau and Rein[9] for dermabrasion or skin-planing. The reason for such 'prophylactic' dermabrasion will be discussed elsewhere. After a biopsy of the edges of one of the abraded and one of the non-abraded incisions had been made, each set of duplicate wounds was closed in one of the following ways:

1. By suturing with No. 5-0 or 6-0 black silk, using a No. 19 cutting needle.

2. By taping with the special adhesive plastic tape kindly provided by Dr. Williamson.* The transparent, specially perforated ½-inch or ¾-inch wide plastic tape was applied as follows:

A 2½"—3" length of tape was used, and one end was applied, with firm pressure, about 1½ inches away from the incision, to provide a firm grip on the skin. Then, by pulling on the free end of the tape, and simultaneously squeezing the wound edges together with the fingers, or by co-apting them with fine forceps, the tape strip was firmly pressed on to the skin on the *other* side of the incision—once the operator was satisfied, on viewing the incision through the transparent tape, that the edges of the incisions were correctly co-apted. Almost hair-line closure was easily achieved with only a little practice (Figs. 3B, 4). We preferred to use a greater number of ¼-inch wide strips (cut from the broader tape) to the use of fewer strips of broader tape, since the narrower tape permitted more precise apposition and greater security.

Successive strips of tape were applied with very narrow intervals between each strip. The ends of the transverse strips of tape were then made more secure, against the possibility of slipping, by 2 broad pieces applied on each side parallel to the incisions and across the ends of all the transverse strips.

It should be mentioned that, since in our experiments there were 4-6 closely neighbouring incisions on each forearm, closure with tape was made under the most difficult conditions; for, as one wound was closed excessive tension was unavoidably applied to the edges of the neighbouring wounds. Moreover, as the subjects were young and healthy, the natural elasticity of the skin and the bellying of the well-developed flexor muscles of the forearm resulted in wide spontaneous gaping of the

*Dr. P. Williamson informed us that the tape is 'self-sterilizing', but could, however, be autoclaved. One of the specimens of tape provided by him (and which closely resembled ordinary plastic adhesive tape available in any stationery store) stood up well to repeated autoclaving. A more recent polythene tape, also made available by Dr. Williamson, did not stand up well to autoclaving. He informs us that further types of tape and adhesive are being manufactured for experimental trials.

However, we have now found that good quality plastic adhesive tape, purchasable at most stationery stores, was quite efficient for closing some of our biopsy wounds. It does not require autoclaving since the adhesive contains phenol and latex, and it is therefore virtually self-sterilizing.

We gratefully acknowledge here Dr. Williamson's kind collaboration and assistance.

incisions (Fig. 3A). Since subcutaneous sutures were never used, on 2 subjects a single and fairly superficial tension suture had to be inserted, in order to appose the edges of the incisions of the wounds, which were finally closed with tape. Such tension sutures, when used on tape-closed wounds, were always removed on the fifth or sixth post-operative day. Bleeding was controlled by pressure with dry swabs, clamps and sutures never being employed for this purpose in these cases.

Dressings of tulle-gras or erythromycin ointment on dry gauze and lint were applied, and these were then covered with a crêpe bandage kept in place by plaster strips at the proximal and distal borders.

The volunteers went about their daily duties, which varied from clerical or laboratory and animal room work to mountaineering (in one case). Thus healing took place under conditions which were far from the surgical ideal of complete rest, making these experiments rigorous tests of the wound closure methods.

The strips of tape were removed completely at the tenth or fifteenth post-operative day. Removal was facilitated by moistening the skin with 95% alcohol, or preferably with ether, when necessary, care being taken to avoid allowing these solvents reaching the incisions. Alternate sutures were removed from the sutured wounds first at 5 and finally at 10 days.

All wounds were examined at 5, 10, 15, 20, 40 and 60 days, and photographed at each of these times. At least 2, and in some instances 3 elliptical biopsies, 5-10 mm. long, 2-4 mm. wide, and down to subcutaneous fat, were taken on 2 or more of the above-mentioned times, while the 'duplicate' set of control wounds, on the same forearm, was allowed to heal without any further interference.

Details of the histological changes in the sutured or taped, prophylactically abraded and non-abraded wounds, as revealed from serial sections of the biopsies will be described elsewhere.

OBSERVATIONS AND REMARKS

Three methods of making observations were used, viz. macroscopic inspection, crude assessments of the tensile strength of the wounds at the time of biopsies and, finally, microscopic observations on serial sections of the biopsy specimens. Observations were continued for 60 days post-operatively, while full clinical notes were made throughout the observation period, at almost daily intervals, after the tenth or fifteenth days.

Macroscopic Findings. As can be seen from Figs. 3-5, the healing of the taped wounds was in every way as good as, and in many respects considerably *better,* than that of the sutured wounds. The edges of the latter were invariably somewhat inflamed and congested, especially in relation to the fine silk sutures (Figs. 3B, C; 4). These reactions were clearly aggravated by the constant use of the incised arms and were most marked at the suture needle puncture wounds. They increased in severity with time until all the sutures were removed on the tenth day. After removal of the sutures, comedo-like keratinized plugs could consistently be seen, even macroscopically (but more clearly with a 10x magnification hand lens) at the suture needle puncture sites (Figs. 1, 3C, 4). The microscopic features of such cysts and 'comedos' (Figs. 1, 2) related to suture needle puncture wounds have already been fully described elsewhere.[2]

The untoward minor inflammatory reactions associated with sutures, as compared with the absence of such reactions in taped wounds, were particularly apparent in one of our Asiatic subjects (Figs. 3B, C). It is well known, to all who have worked on pigmented skins, that irritation and inflammation induce increased pigmentation. Such pigmentation was well marked about the sutured wounds and was absent from the taped wounds, which healed with a hair-line scar (Figs. 3-5).* As shown in Fig. 4, reactions to sutures produced a distinct erythema, even in non-pigmented skins, with subsequent exfoliation—both of which reactions were absent from taped wounds (Fig. 4).

So impressed were we with the results obtained with tape closure in our first volunteers, that we soon discarded suture of biopsy wounds in favour of tape closure. This was done not only because of the better results with the tape, but also because of the fact that in suturing biopsy wounds at the 5th (or even at the 10th) post-operative days it was very difficult to avoid splitting the partially healed wound, while pushing the suture needle through the skin. Closure of biopsy wounds with ¼-inch wide tape strips, as described here, not only speeded up and considerably facilitated the biopsies, but eliminated the complication of splitting the original incisions, the extra suturing (with associated irritation) and the need to remove these sutures later—thus

*Details about pigmentation, etc. in the prophylactically *abraded* incisions will be recorded elsewhere.

contributing to the far better end results obtained with tape (Figs. 3C, 5).

We found very little discharge beneath the tape, even in prophylactically abraded incisions. None of the subjects complained of any irritation or discomfort attributable to the plastic tape used in the wound closure; nor was there any accumulation of sweat under the tape, despite the fact that these experiments were conducted in actively working subjects in the humid, tropical climate of Durban. Ordinary zinc plaster or Elastoplast (used for keeping the crêpe bandages from slipping) did, on the other hand, cause some itching and discomfort in several of our subjects.

In the light of our experiences, we intend making further trials in major surgical operations and would like to omit *all* dressings other than the tape used for wound closure, whenever this is feasible. We have found that covering the taped wounds with a second layer of the more flexible polythene tape provides an excellent, airtight, comfortable dressing which has the added advantage of allowing constant scrutiny of the incisions without disturbing either the patient or the wound.

Tensile Strength of Wounds. In respect of the tensile strength of the wounds closed by different methods, the prophylactically abraded wounds were by far the strongest and, at 5 or 10 days, the taped and non-abraded wounds were weakest. As judged by tendency of the wounds to split at biopsy on the 5th or 10th day, the relative tensile strength of the wounds was thus, in order of increasing strength:

1. Taped and non-abraded;
2. Sutured and non-abraded;
3. Taped and abraded;
4. Sutured and abraded.

The reasons for the consistently greater tensile strength of abraded wounds became apparent only on microscopic study of biopsy specimens, details of which will be described elsewhere, together with the rationale for prophylactic abrasion before incising the skin. It seemed that the slightly greater strength of the sutured wounds was attributable not only to the presence of sutures, but also, perhaps, to the peri-sutural connective tissue reactions acting as extra 'stays' for the incision line. Both sutured and taped wounds tended to 'spread' after removal of the tape or sutures. This was especially evident in *longitudinally* placed wounds, and most marked if tape was removed before the 5th post-operative day (*cf.* Figs. 3C, D). This tendency of wounds (or scars) to 'spread' after the 10th or 15th post-operative day is, of course, far greater in the forearm skin, more particularly in longitudinally directed incisions and especially so in our young volunteers with highly elastic skin and well-developed forearm flexor muscles, who used their hands continually from the moment the original or biopsy operations were concluded.

If the original wounds were re-taped (after photography and biopsy) and the tape retained both on the initial and on biopsy wounds, preferably until the 15th post-operative day, then perfect hair-line scars were obtained which did not widen thereafter (Figs. 4, 5).

One of our subjects (the mountaineer) removed his dressings too early and was so interested in the results of the experiment that he daily examined and frequently manipulated the healing wounds after the dressings had been removed on the 10th post-operative day. In this subject, the scars in *all* the original incisions, made longitudinally along the forearm, became hypertrophic. The *transverse* biopsy wounds in this subject, however, healed well, and with thin, normal scars.

The fact that the tensile strength of both sutured and of taped (non-abraded) wounds was very poor (especially at the 5th post-operative day) can easily be explained (and at the same time confirms our original observations recorded elsewhere[1, 2]) by the fact that, *microscopically,* connective tissue repair of an incision was found to *succeed* the epithelial bridging of incisions by several days, and become well marked, in human skin, only between the 6th and 12th post-operative days. In the light of our observations, we think that wound edges should be supported for at least 15-20 days in order to allow dense collagenization of the incised dermis. This will contribute much towards preventing later widening of scars.

DISCUSSION

Whilst we appreciate that the above findings are based on the study of relatively small incisions, which are not quite as deep as the usual surgical incision (i.e. only down to subcutaneous fat and not to or through the fascia and/or muscle), we feel justified in drawing attention to the fact that the incisions were made in a skin site which does not give the best type of scar, even under ideal conditions. Moreover, the longitudinal placing of incisions in some of our subjects was done purposely, in order to put the methods of wound closure under the severest possible test. The condi-

tions of these tests of wound closure methods were made more rigorous by the fact that in no case was a surgically treated part placed at rest and, in fact, the experimentally incised forearms were constantly in use (in 2 cases vigorously so) from the moment of completion of the operations.

For general surgical practice, in dealing with incisions extending through all the layers down to peritoneum, the usual sutures required for the closure of deep layers such as peritoneum, muscles and their sheaths, deep fascia, etc. sutures are obviously still necessary. However, for the closure of incisions in the skin itself, only 2 or 3 widely spaced tension sutures or subcuticular stitches would be necessary in *long* wounds. For the rest, speedier and much better apposition of incised edges can be achieved by completing skin closure with plastic tape according to the method here described. Spread of infection along sutures, suture puncture scars, etc. would also be avoided. Drains, when required, could always be placed between strips of tape and, when superficial, could easily be taped into position. Tape closure should also prove particularly valuable, if and when desirable, for closing gaps left by drains.

Besides its surgical practicability, if not actual desirability, in terms of end results for the healing process itself, tape closure is extremely simple and rapid. Moreover, the use of costly sutures and suture needles is cut to a minimum, making tape closure preferable on purely economic grounds. The patient is spared the discomfort, or even pain, attending removal of sutures, and the usually overworked nursing staff is saved the valuable time and effort of taking down dressings repeatedly in fulfilment of the common present-day surgical practice of removing alternate sutures at intervals. It is anticipated that healing should also be speedier, purely by virtue of the diminished interference with the operation site, more especially if tape closure is used alone and without any dressings, as suggested here.

In addition to all the above advantages, theoretical and factually based reasons have been provided (from a microscopic study of the healing process in sutured skin wounds) for diminishing the use of sutures in major surgical incisions and discarding sutures entirely for skin closure wherever possible. For all the foregoing theoretical and practical reasons, and because of the extreme simplicity and speed, transparent adhesive plastic tape would seem to be a most acceptable alternative for closing skin wounds, and highly desirable for rapid wound closure in severely injured and shocked patients, and as a routine procedure in general practice for minor injuries in casualty wards.

For plastic surgery, where cosmetically pleasing end results are usually aimed at, tape closure of wounds (especially with prophylactic abrasion) will, we hope, provide the ideal method of skin wound closure. As shown by us elsewhere,[1, 2] once the stratum papillaris of the dermis is punctured and the puncture wound kept open for some hours, a scar is an inevitable end result, even if only punctate. Besides, we have several cases on record where susceptible individuals have developed keloids, like a row of beads, in each and every one of the punctate suture scars. In such keloid-formers tape closure of skin wounds would seem to be the method of choice.

Other uses for adhesive tape in surgery are anticipated, especially the fixing of split-skin and other free grafts to recipient sites.

CLINICAL APPLICATIONS

The clinical use of tape has now been tried in our wards for several months, and our observations on its use indicate that there are certain limitations as well as great advantages. It is particularly useful in bringing together an incised wound where there is no skin loss or skin rotation, particularly on flat areas. In these cases it has been our practice to bring the deeper layers of dermis together by means of catgut sutures, the knots of which are placed in subcutaneous fat, and the surface epithelium is brought together meticulously by means of transparent adhesive tape. In long incisions, fine epidermal sutures on eyeless needles are utilized at intervals of about 2 inches, depending upon the tension of the skin, and tape is applied between these sutures. These sutures may often be removed within 48 hours and replaced by tape.

In incisions or excisions of skin which disturb superficial tensions because of rotations and advancements, it is advisable not to limit the same number of sutures placed· but it is possible to remove them at a much earlier date than heretofore and to replace them with tape. This minimizes cross-hatch scars even in such circumstances.

Over a period of several months only one patient has shown skin sensitivity to the tape used, and it was of a very mild nature. This is in contra-distinction to the use of conventional adhesives, where sensitivity is frequently encountered. Transparent tape can therefore

be left on the skin for a long period, even as long as a fortnight, without discomfort to the patient. Such a routine is extremely useful, particularly in areas where movement is to be expected, as the tape minimizes pull on the cut edges, thus preventing lateral stretching of the scar.

The taping of wounds is particularly useful in first-aid work, especially in children. Cases of dog-bite and cuts which previously would have required hospitalization, anaesthesia and surgery under unfavourable emergency conditions, have been treated in our consulting rooms with taping, successfully and without risk.

There is no doubt that this method of closure will play a great part in the treatment of war injuries and trauma where time is an important factor, and where operating conditions are unfavourable.

Apart from normal cleansing of the wound, the wound must be dry before tape can be applied, otherwise blood and serum will float it. Even after the wound is dry it is necessary to leave spaces between the tape for seepage. The tape can be removed as often as is necessary, without pain or discomfort, and can be replaced equally effectively. This is an advantage after treatment under local anaesthesia, when there is a tendency for secondary oozing to occur after the adrenaline action has worn off. It is our practice in these cases to detain the patient until this oozing has occurred, so that he can be sent home with a secondary taping which is usually dry and clean.

Any form of transparent, adhesive tape is suitable for flat areas, but on curved areas a certain amount of elasticity is required. Tapes with such textures are available commercially.

SUMMARY AND CONCLUSIONS

1. Previous microscopic analysis of the repair process in surgical incisions had disclosed several hitherto not generally recognized phenomena, including invariable vigorous epithelial down-growths into the dermis, both in the line of the incision itself and along the sutures.

These epidermal reactions, especially well marked in relation to the suture needle puncture wounds, always complicate wound healing considerably and contribute much to the ultimate scar. Consequently, methods for sutureless closure of surgical incisions were sought.

2. After considering several other methods described in the literature for closing skin incisions without sutures, we adopted the use of a transparent plastic adhesive tape with a special adhesive suitable for human skin. This tape can be autoclaved and perforated to permit drainage.

3. Results here reported are from initial experiments conducted on 5 ambulant and active human volunteers, entailing the experimental infliction of several incisions through the skin of the forearm and down to subcutaneous fat. These incisions were closed with adhesive plastic tape, and the results with this type of closure were compared with those obtained in another equivalent incision in the same subject, but closed with multiple fine silk sutures. Frequent observations (up to the sixtieth post-operative day) have thus far been made.

4. The disadvantage of suturing skin wounds and the advantages of tape closure are reviewed, in terms of speed, avoidance of pain, expense of suture materials and dressings, the time of nursing staff and the promotion of rapid healing through minimal post-operative interference with wounds.

5. A method for using adhesive tape for closing major surgical incisions is suggested.

6. These preliminary tests show that, at least in the type and location of wound here studied, closure of skin incisions by transparent plastic adhesive tape was *superior* to closure with sutures.

7. Further extended trials of transparent adhesive plastic tape for closing skin incisions in major surgery, in plastic surgery on keloid-producing subjects, and for applying free skin grafts, in general practice, in all emergencies and casualty wards can be strongly recommended on both practical and theoretical grounds.

8. The clinical applications of the taping closure of wounds are reviewed.

OPSOMMING

1. Vroeëre mikroskopiese ontledings van die herstelproses ná chirurgiese snedes het 'n hele paar verskynsels wat tot dusver nie algemeen herken is nie, aan die lig gebring, insluitende onveranderlike kragtige epiteel-afgroeiings in die dermis in, sowel op die lyn van die snede self as langs die steke.

Hierdie opperhuidreaksies wat veral opvallend is in verhouding tot die prikwonde wat deur die wondnaald gemaak word, bemoeilik steeds die genesing van die wond, en dra veel tot die uiteindelike vorming van littekens by. Gevolglik is daar gesoek na metodes vir die sluiting van chirurgiese snedes sonder steke.

2. Ná oorweging van etlike ander metodes vir die sluiting van velsnedes sonder steke wat in die literatuur beskryf word, het ons oorgegaan tot die gebruik van 'n deurskynende plastiekkleefband met 'n spesiale kleefmiddel wat geskik vir die menslike vel is. Hierdie band kan in 'n autoclaaf gesteriliseer en geperforeer word om dreinering toe te laat.

3. Die resultate wat hier gerapporteer word, is verkry na aanvanklike proefnemings met 5 rondlopende en aktiewe menslike vrywilligers. Dit het die proefondervindelike aanbring van etlike snedes in die vel van die onderarm en tot by die subkutane vet meegebring. Hierdie snedes is gesluit met plastiekkleefband, en die resultate wat met hierdie soort sluiting verkry is, is vergelyk met dié wat verkry is nadat 'n ekwivalente snede by dieselfde pasiënt met veelvoudige fyn syhegtings materiaal toegewerk is. Herhaaldelike waarnemings (tot op die sestigste dag ná die operasie) is tot dusver gedoen.

4. Die nadele van die steekhegting van velwonde en die voordele van bandsluiting word in oënskou geneem, in terme van snelheid, die voorkoming van pyn, die onkoste van hegtingsmateriaal en verbindsels, die tyd van die verpleegpersoneel, en die bevordering van vinnige genesing deur minimumversteuring van die wond na die operasie.

5. 'n Metode om kleefband vir die sluiting van groot chirurgiese snedes te gebruik, word aan die hand gedoen.

6. Hierdie voorlopige toetse toon aan dat, wat betref die tipe en die ligging van die wonde wat hier beskryf word, die sluiting van velsnedes met deurskynende plastiekkleefband *beter* was as sluiting met 'n hegtenigsmateriaal.

7. Verdere uitgebreide proefnemings met deurskynende plastiekkleefband vir die sluiting van velsnedes ná groot operasies, ná plastiese chirurgie met keloïedproduserende pasiënte, en vir vrye huidinplantings, in die algemene praktyk, in alle noodgevalle, en in ongevallesale kan sowel op praktiese as teoretiese gronde sterk aanbeveel word.

8. Die kliniese toepassings van die sluiting van wonde met band word in oënskou geneem.

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Eli Lilly & Company kindly provided the erythromycin ointment here used.

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COARCTATION OF THE AORTA

ASSOCIATED WITH CONGENITAL POLYCYSTIC KIDNEYS

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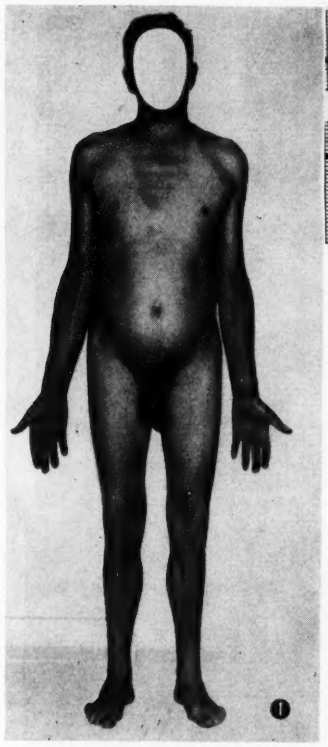
Coarctation of the aorta is a well described congenital anomaly, but its association with extra-cardiac abnormalities is extremely rare.

CASE REPORT

A 44-year-old European male was admitted to the Johannesburg General Hospital complaining of vomiting, diarrhoea and cramps in the legs of some 8 hours' duration. He had suffered from hypertension for many years and had been treated with a low salt diet and antihypertensive drugs. On admission he was distressed and dehydrated and a diagnosis of gastro-enteritis was made; 24 hours later, after correction of his dehydration, he was able to give the following history.

He had undergone many routine medical examinations and had been passed A1 during World War II. In 1937 he was refused a life insurance policy because of his high blood pressure. As long as he could remember he had suffered from cold feet and cramps in the legs, although these were never as severe as those which he had experienced just before admission. Throughout adult life he had been self-conscious about the disproportion between his upper and lower extremities and had been reluctant to wear short trousers.



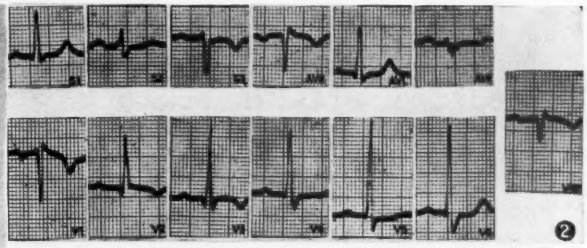


Fig. 1. Note the disproportion between the upper and the lower limbs.
Fig. 2. The electrocardiographic tracings indicate marked anti-clockwise rotation (qR pattern present in leads V2 to V6); partial right bundle branch block (rsr pattern in leads V1 and V4R, late S wave in the left venticular leads V3—V6 and absence of a prominent R wave in lead V4R); and suggestive left ventricular hypertrophy (the sum of the extent of the deepest S wave in right venticular leads, i.e. V1 in this case, together with that of the tallest R wave in left ventricular leads, i.e. V5 in this case equals 37 mm., which is just above the upper limit of normal).

Physical examination revealed a well-built adult male with obvious disproportion between the upper and lower limbs (Fig. 1), the latter being short and thin in comparison with the arms.

Measurements: Height—73½ inches; span —80 inches; top of pubes to ground—38½ inches.

An arcus senilis was present. The optic fundi showed a grade II retinitis. The radial pulses were collapsing in type and prominent locomotor brachiali were noted.

Blood Pressures: Right arm—210/110 mm. Hg; left arm—210/90 mm. Hg; right leg—150/100 mm. Hg; left leg—150/100 mm. Hg.

Examination of the chest revealed marked pulsation in the suprasternal notch and both supraclavicular fossae. The maximum cardiac impulse was not seen or felt and there were no praecordial thrills. Auscultation of the aortic area revealed a grade III crescendo-decrescendo systolic murmur which was propagated into the neck and down the left sternal border. In addition a grade II early diastolic murmur was heard in the aortic area with radiation down the left sternal border. These murmurs were less audible in the mitral and pulmonary areas. The pulmonary second sound was normal. No classical Gibson murmur was heard. There was no disturbance of cardiac rhythm.

Arterial pulsations were both seen and felt over the medial borders of both scapulae. The pulses of the lower limbs were diminished and *delayed* compared with those of the upper limbs.

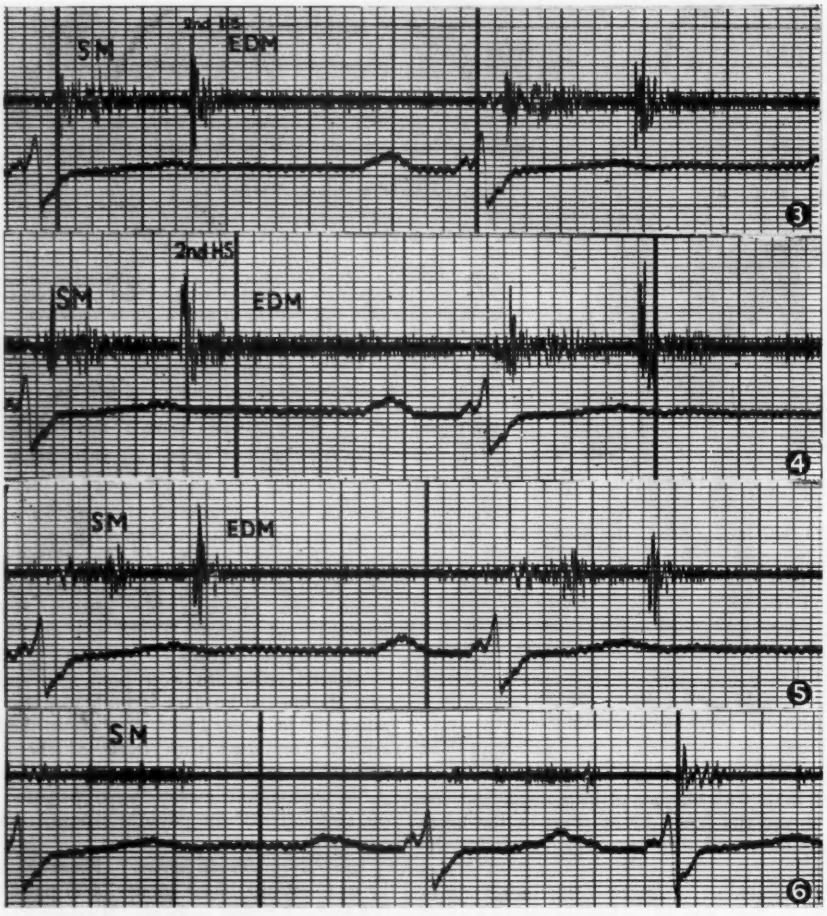
No abdominal masses were palpated and the remainder of the physical examination was essentially negative.

Laboratory Investigations: Haemoglobin—15 g. %. White blood count, 7,600 per c. mm. Differential count, normal. Erythrocyte sedimentation rate, 1 mm. per hour (Westergren). Blood urea, 81 and 69 mg. per 100 ml. Wassermann reaction, negative. Urine: microscopic, chemical and cultural examinations showed nothing abnormal.

The electrocardiogram (Fig. 2), indicated marked anti-clockwise rotation, left ventricular hypertrophy and partial right bundle branch block.

Phonocardiogram: (Figs. 3-6).

Radiological Examination (*Dr. I. Friedman*): Figs. 7, 8. The heart is enlarged in its transverse diameter (cardiac: thoracic ratio—57.6). The contour is left ventricular in shape. The hilar shadows are within normal limits. The ascending aorta is unfolded. The vascular band is widened. In the straight view (Fig. 7) the impression of a



S M = Systolic murmur; E D M = Early diastolic murmur; H S = Heart sound.

Fig. 3. A phonocardiogram of the aortic area showing a decrescendo systolic murmur and an early diastolic murmur.
Fig. 4. A phonocardiogram of the pulmonary area showing a systolic murmur with midsystolic accentuation diminishing in intensity and stopping short of the second heart sound which is split and followed by a decrescendo early diastolic murmur which occupies practically the whole of diastole.
Fig. 5. A phonocardiogram of the left sternal border showing a soft first heart sound with a crescendo-decrescendo systolic murmur and an early diastolic murmur.
Fig. 6. A phonocardiogram of the mitral area showing a late crescendo-decrescendo systolic murmur and no diastolic murmur.

large aortic knuckle is given (A). Below this a double density can be seen (B). In the penetrated view (Fig. 8) it is seen that the so-called aortic knuckle is a false one and is due to a dilated left subclavian artery (A). Below this a smaller density can be seen which is the aortic knuckle (B).

In the left oblique view gross left ventricular enlargement is noted. The right ventricle is not enlarged.

In the right oblique view there is no displacement of the barium-filled oesophagus and the pulmonary conus is within normal limits. No definite calcification can be seen within the aorta.

In the survey of the chest, gross rib notch-

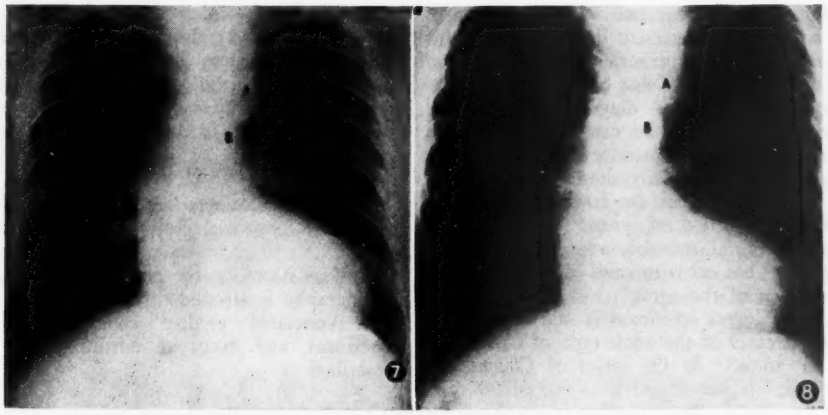


Fig. 7. X-ray of the chest showing a false aortic knuckle (A) and a double density (B). Note also the marked rib notching and the gross left ventricular hypertrophy.
Fig. 8. A penetrated view showing the dilated left subclavian artery (A) and the aortic knuckle (B). Note the gross left ventricular hypertrophy.

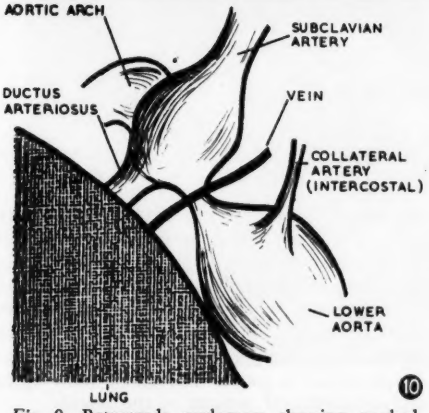


Fig. 9. Retrograde pyelogram showing marked bilateral polycystic kidneys.
Fig. 10. Diagram of the thoracoscopy findings.

ing is noted on both sides extending from the 4th to the 9th ribs (Fig. 7).

Conclusion: There is a coarctation of the aorta with a gross enlargement of the left ventricle. This is suggestive of an aortic valvular lesion. The pulsations in the ascending arch were collapsing in type, indicating aortic incompetence.

Excretory and retrograde pyelography (Fig. 9) revealed gross bilateral polycystic kidneys.

Thoracoscopy (*Mr. P. Marchand*) (Fig. 10): 'The actual coarctation was string-like in nature and the base of the left subclavian artery was greatly dilated. The aorta below the coarctation appeared to be of the same size as above the constriction. A large collateral intercostal artery stemmed from the lower aorta and passed upwards. A vein crossed the actual stricture and passed between the lower aorta and a ductus arteriosus which seemed to be patent.'

COMMENT

This patient shows the well-developed physique so frequently found in coarctation of the aorta. The disproportion between the upper and lower extremities is strikingly illustrated, his span exceeding his height by 6½ inches.

It is interesting to observe that it was only on comparison with the pulsations in the upper extremities that the diminished pulsations in the lower extremities became evident. However, the *delayed* pulsation in the lower extremities was most apparent in this case.

Bicuspid aortic valves is the commonest

cardiac anomaly associated with coarctation of the aorta. In was present in 11% of Abbott's series,[1] 42.3% in the series of Reifenstein *et al.*[2] and in 18.5% in that of Clagett and Jampolis.[3] Clinically, a diagnosis of bicuspid aortic valves cannot be made with certainty. In this case the lesion was diagnosed on the basis of the loud early diastolic murmur at the base of the heart, the large pulse pressure and the presence of gross left ventricular enlargement. Gross left ventricular enlargement does not occur in cases of uncomplicated coarctation of the aorta.[4]

Patent ductus arteriosus is said to occur in 10% of cases of the adult type of coarctation of the aorta.[5] In the series of Clagett and Jampolis[3] it was found in 3 out of 70 cases and they make note of the fact that one patient presented no diastolic murmur. In this case the ductus arteriosus was seen on thoracoscopy and seemed to be patent although no Gibson murmur was detected either on auscultation or phonocardiography. It may, however, be inferred that, because the pulmonary and hilar vessels were not unduly prominent, the flow through the ductus was minimal.

Coarctation of the aorta with associated extra-cardiac congenital abnormalities is extremely rare. Clagett and Jampolis found 3 cases (undescended testis, double vagina and cervix, and an ectopic left kidney) in their series of 70. In a search of the literature we have not encountered a case associated with polycystic kidneys. In this case, abdominal palpation did not reveal any abnormal masses, the polycystic kidneys being discovered on excretory pyelography to ascertain renal function. The presence of these polycystic kidneys was the factor which militated against the decision to correct the coarctation surgically. The association may be more common than has hitherto been thought and the necessity for routine pre-operative pyelography in every case of coarctation of the aorta is thus evident.

SUMMARY

1. A case of coarctation of the aorta with associated congenital polycystic kidneys is discussed.

2. The necessity for routine pre-operative pyelography is stressed.

3. Associated cardiac anomalies (ductus arteriosus and bicuspid aortic valves) are described.

OPSOMMING

1. 'n Geval van koarktasie van die aorta met geassosieerde aangebore policystiese niere word bespreek.

2. Die noodsaaklikheid van roetine-vooroperasie-pyelografie word benadruk.

3. Geassosieerde hart-anomalieë (ductus arteriosus en tweeslippige aortavliese) word beskryf.

We wish to thank Drs. K. Mills and T. Schneider for permission to publish this case. Our thanks are also due to Mr. P. Marchand for the thoracoscopy, Dr. J. Greenstein for the phonocardiogram and Dr. I. Friedman for the radiological report. We are indebted to Mr. A. M. Shevitz for the photographic reproductions.

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'KNOPIE-SPIDER' BITE IN SOUTHERN AFRICA

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Cape Town

The earliest report of spider bite in South Africa appears to have been made by Thompson (1827), quoted by *Nathanial Isaacs,*[1] who stated that a Native woman was bitten on the toe by a small spider and that she died shortly afterwards. Although Thompson gives no description of the spider, in view of the toxicity of the bite it was almost certainly one of the South African species of Latrodectus.

In 1902 Pickard-Cambridge[2] described 2 species of *Latrodectus, L. indistinctus* and *L. concinnus.* The latter was shown by Smithers[3] to be a synonym of *L. geometricus.* In 1929 MacPherson[4] of Stellenbosch described a series of 6 cases of spider bite, occurring in the Stellenbosch area, which he ascribed to the bite of *Latrodectus maculata,* which was later identified as *L. geometricus,* a species of Latrodectus which is found throughout the tropical and semi-tropical regions of the world.

L. indistinctus was first incriminated as a cause of serious cases of spider bite in the

Cape, by Finlayson,[5-6] who showed that the female of both *L. indistinctus* and *L. geometricus* could produce serious illness in man. The females of both of these species of Latrodectus had been commonly called 'knopie-spider' or 'knopie-spinnekop', or 'button spider'. Finlayson[9] described a series of 18 cases of spider bite, occurring in the Cape Province, in 2 of which the spider responsible was identified as *L. indistinctus*. A further case of spider bite in the Cape was described by Cole[7] (Wynberg, C.P.). In this case the bite was due to *L. geometricus*.

APPEARANCE, DISTRIBUTION AND HABITAT

The female *L. indistinctus* (Fig. 1) may be about 20 mm. long and has a well rounded abdomen, from which it derives the name 'knopie-spider' or 'button-spider'. It is usually jet-black or dark-brown in colour and the dorsal surface of the abdomen is frequently characterized by irregular white or yellowish spots, more or less indistinct (hence *indistinctus*), and which are entirely absent in some specimens. Many specimens show a dull red or orange spot about 1 mm. in diameter on

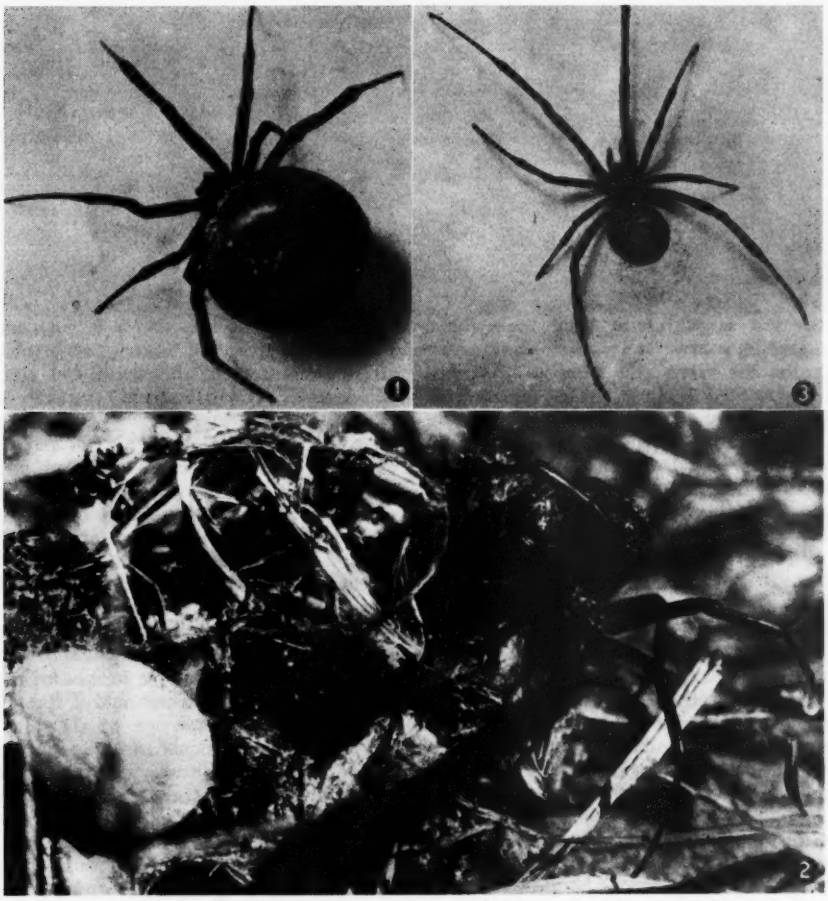

Fig 1. Female *L. indistinctus* showing irregular markings on the dorsum (× 4).

Fig. 2. Female *L. indistinctus* in her nest. The egg sac is visible in the nest (at the left of the photograph).
Fig. 3. Female *L. geometricus* (*L. concinnus*). Two-thirds natural size.

the dorsum at the posterior end of the abdomen. Smithers[3] described a variety of *L. indistinctus* which he named *L. indistinctus* (var. *Karooensis*). This variety is characterized by a distinct red medial dorsal longitudinal band, on the dorsal surface of the abdomen. The anterior end of this band is frequently produced laterally into 2 arms, forming a T-shaped marking.

L. indistinctus is most commonly found in the wheat belts of the Western Province, but has been described throughout the Union of South Africa and the Rhodesias. Proven cases of spider bite due to *L. indistinctus* have, however, only been reported from the wheat lands of the Western Province and of the Eastern Orange Free State. In some parts of the St. Helena Bay area in the Western Cape, the spiders are so numerous that after the wheat has been harvested and loaded on carts, the cart is backed up to a fire in the farm-yard. The spiders on the surface of the wheat are then scraped off with twigs into the fire before the wheat is off-loaded.

L. indistinctus usually prepares a nest about 3—4 inches in diameter. This nest is placed at the base of plants in the wheat fields and is frequently found between 2 or 3 plants to which the web is attached. The web is very strong and large insects have been found entangled in it.

During the harvest the nests are disturbed and exposed to the sun. The spiders seek shelter in the sheaves of wheat which are in the fields to dry. When the farm workers collect these sheaves under their arms, they may come into contact with a spider which may inflict a bite. The majority of bites by *L. indistinctus* appear to occur in this manner, but cases have been reported where the spider has apparently inflicted a bite without provocation. The writer can corroborate these reports from painful personal experience, having been bitten by a young female *L. indistinctus* which escaped from a jar in which an egg sac had recently hatched. The first indication that a spider was at large was the experience of a painful sensation on the dorsum of the hand, when it was observed that a young spider had settled and inflicted a bite.

The egg sacs of *L. indistinctus* (Fig. 2) are spherical in shape, smooth on the surface and about 1—1.5 cm. in diameter. At least 10 egg sacs may be produced by the female *L. indistinctus* after one fertilization, and each egg sac may contain 170 eggs.

Most of the cases of spider bite due to *L. geometricus* have been reported as occurring in vineyards of the Western Province. This spider makes its nests, commonly, in and around buildings, round barns, stables, garden boulders, under the bark of trees, under stones and in tufts of grass, herbs and vines. The reported cases have occurred in summer and autumn when vineyards are being worked and the grapes harvested. No fatal cases of spider bite by *L. geometricus* have been reported.

The female *L. geometricus* (Fig. 3) is about 10-12 mm. long and varies in colour from light grey to brown or black. The abdomen is rather pear-shaped and is characterized by 3 triangular black spots with a white border which are situated medially on the dorsum.

Posterior to these, also on the dorsum, is an elongated spot of the same colour. On either side of these spots, extending obliquely over the dorsum, are 3 or 4 similar markings. In different specimens the markings vary considerably and in some specimens are barely recognizable. On the ventral surface of the abdomen is a dumb-bell shaped area varying in colour from orange to bright red.

The egg sacs of *L. geometricus* are about 1 cm. in diameter and are characterized by small protuberances (Fig. 4). They are whitish grey in colour. The web is small and strong and is placed just outside the domicile of the spider.

This species of Latrodectus is not confined to Southern Africa but has been reported from all tropical areas of the world and also the U.S.A. and Southern Europe.

TOXICOLOGY AND PHARMACOLOGY

Whilst is had long been known that 'knopie-spider' bite could produce serious symptoms and even death, it was not until 1936 that Finlayson[5] showed that extracts of the cephalothoraces of the South African species of Latrodectus which had been identified as 'knopie-spiders', contained a potent venom. It was shown that the venom of *L. indistinctus* was more potent than that of *L. geometricus*, the M.L.D. of the venom of the former for rabbits being 3 mg. as against 12 mg. of the venom of the latter.

The symptoms produced in man by the bite of the South African species of Latrodectus, consist of excruciating cramp-like pains in the limbs, chest and abdomen. There is frequently a feeling of painful tightness in the chest and a fear of impending death. The face is grey and covered with perspiration and the patient may groan or scream. In some cases abdominal rigidity is observed and on occasions may be mistaken for an acute abdominal condition, which it so closely resembles that on occasions laparotomy has been carried out in the absence

Fig. 4. Egg sac of *L. geometricus* (*L. concinnus*), showing the characteristic protuberances (× 4).

of a definite history of spider bite. The patient usually perspires profusely and salivates excessively. The temperature may be subnormal and may rise to 102—103° F. The reflexes are frequently over-active and the patient is often cyanosed.

Nausea and vomiting may be present and death may ensue from heart or respiratory failure. The symptoms usually start within a few minutes of the bite and within half an hour the patient may be unconscious. In the case of *L. geometricus* bite the symptoms are similar to but less severe than those following the bite of *L. indistinctus*. Apart from a feeling of weakness and malaise, the patient is usually recovered within 24 hours.

The writer, when bitten by a young female *L. indistinctus*, first noted a sharp stabbing pain, at the site of the bite on the dorsum of the right hand, which was shortly followed by a painful ache which spread down the fingers and involved the whole hand. The skin on the dorsum of the hand commenced to perspire and these symptoms, which remained localized, persisted for 48 hours. As the spider which inflicted this bite was only a few days old and about 1 mm. in diameter, the intensity of the symptoms produced by a well developed female about 20 mm. in diameter, can well be imagined.

Investigation of the pharmacological properties of *L. indistinctus* venom by Shapiro, Sapeika and Finlayson,[8] showed that it produced a depression of the respiration, and of the heart and its conducting tissues. It was concluded from results of this investigation (which was carried out on rabbits, cats and *Xenopus laevis*) that death following the bite of *L. indistinctus* or 'knopie-spider' is due not only to the depressant effects of the venom on the respiratory system, but also to its depressant action on the heart and its paralysing effects on the peripheral vasculature.

Finlayson[6] was able to show by means of cross-neutralization and precipitin tests that *L. indistinctus* venom not only contains the same antigens as does *L. geometricus* venom, but that it also contains an additional antigen. Antisera prepared against *L. indistinctus* venom could therefore be used in the treatment of spider bite whether due to *L.Indistinctus or L.geometricus*. Experiments carried out by Finlayson and Hollow[9] using purified *L.mactans* (*black widow spider*) antiserum concentrate,

showed that this serum was effective in neutralizing the venom of *L. indistinctus* and in protecting mice against the bite of this spider. These results indicated that *L. mactans* and *L. indistinctus* venoms contain a common antigen, and unless the venom of *L. mactans* contains additional antigens, the antigenic composition of the 2 venoms is identical, as complete protection against the bite of *L. indistinctus* was obtained by the injection of *L. mactans* antiserums. Further experiments on the protective action of *L. indistinctus* antiserum against *L. mactans* venom must still be carried out before the exact relationship between the 2 venoms can be determined.

TREATMENT

The treatment of spider bite and, in particular, of bite due to spiders of the genus *Latrodectus*, has until recent years been largely empirical and symptomatic. Where the bite was on a limb, the bite was excised and potassium permanganate rubbed into the wound after the application of a tourniquet, which was loosened at intervals, but immediately tightened on the appearance of general symptoms. The general symptoms were usually treated by the judicious use of morphine and atropine, which were sometimes given along with pituitrin and adrenaline to combat shock. Dehydration, due to vomiting and perspiration, was combated by saline *per rectum* and intravenously and, if the patient was greatly collapsed, venesection was carried out to relieve the right side of the heart. Respiratory distress was treated with oxygen containing 5% carbon dioxide. In some cases the administration of paraldehyde *per rectum* was claimed to produce good results.

Before the introduction of specific antiserum for the treatment of spider bite, cases were sometimes treated with cobra and puff-adder antiserum. Finlayson[6] showed that these antisera had no neutralizing action on *L. indistinctus* venom and were therefore useless in treatment of "knopie-spider" bite. He prepared a specific antiserum from *L. indistinctus* venom by the inoculation of goats and advocated the use of this serum in the treatment of spider bite due to either *L. indistinctus* or *L. geometricus*. This antiserum was issued on request to magistrates and District Surgeons throughout the Union. In 1937 Finlayson[10] published a detailed report on the effect of the antiserum in the treatment of 18 cases of spider bite, all of which recovered following treatment with the serum. Before the introduction of this serum, details of fatal cases following 'knopie-spider' bite were not infrequently published in the local Press. In 1934, four such deaths said to be due to spider bite were notified in the Union. Since the introduction of the specific antiserum in 1935, the writer has been unable to trace any records of fatal cases of spider bite in South Africa. Between 1935 and 1955 records of 77 cases of spider bite treated with specific antiserum have been obtained and some of these records indicate remarkable recoveries shortly after the injection of the serum.

During the period 1936-1945, 762 phials of antiserum were issued from the Union Health Department Laboratory at Cape Town and from 1949-1953, 1,794 ampoules were issued by the South African Institute for Medical Research, Johannesburg, which now manufactures and issues the serum in Southern Africa. It would appear from these figures that there has been a marked increase in the demand for *L. indistinctus* antivenine over the 4-year period 1949-1953, as compared with the 7-year period 1939-1945. This increased demand, along with the reports which have been received of the results of treatment, would indicate that the use of *L. indistinctus* antiserum is very effective in the treatment of 'knopie-spider' bite in the Union and should be the treatment of choice when available. This antiserum also appears to be effective against the bite of *Harpactirella lightfooti* (Finlayson[11]), although the venom of this spider has not yet been isolated.

OPSOMMING

Die voorkoms, verspreiding en verblyfplekke van die knopiespinnekop word in oënskou geneem.

Twee variëteite van hierdie spinnekop, saam met hul eiersakkies, word geïllustreer.

Die toksikologie en die farmakologie van knopiespinnekopgif word beskryf, en die behandeling met 'n spesifieke antiserum van die bytplekke wat noodlottige gevolge kan hê, word uiteengesit.

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REVERSIBLE HEART FAILURE

AN UNUSUAL CASE

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and

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L. H., a male African aged 40 years, was admitted to Baragwanath Hospital in 1953, suffering from scurvy. Routine X-ray of his chest was normal. He was discharged 14 days later and was seen at intervals during the next 2 years when he appeared quite well. He was readmitted on 15 July 1955 complaining of breathlessness for the previous 4 days.

He was dyspnoeic and in gross congestive cardiac failure. He had a hypodynamic circulation, viz. cool hands and a low blood pressure (90/70 mm. Hg.) and pulsus paradoxus. Temperature: 98.6° F. Pulse: 108 per minute. His heart was enlarged and a heave was palpable retrosternally but not at the apex. The heart sounds were muffled but closed. X-ray showed generalized enlargement of the heart and minimal pulmonary engorgement (Fig. 1). The E.C.G. showed non-specific T-wave inversions.[1]

The etiology of his heart failure was not obvious and was considered to be either nutritional heart disease or tuberculous pericarditis, a common diagnostic problem amongst Africans. Since the shape of his heart was not typical of effusion, pericardial aspiration was not attempted as we have seen fatalities from this procedure in cases of nutritional heart disease. He was treated with mercurial diuretics.

Over the next 10 days the patient's condition deteriorated. He became more engorged, developed gallop rhythm and a temperature ranging from 99-101° F.

The X-ray appearance of his heart began to change. A localized bulge appeared at the left middle arc of the heart shadow. He was then digitalized. One month after admission he was no better, the signs of venous congestion were unchanged and he still had a raised temperature. He had, however, developed the following new signs:

1. An area of visible pulsation of the chest wall above the left nipple;
2. Paroxysmal auricular tachycardia lasting 10 days;
3. X-ray evidence of a rapidly growing mass at the left cardiac border (Fig. 2).

Radioscopy showed the tumour to be lying in the situation of the left auricle or upper part of the left ventricle posteriorly; it did not pulsate (Fig. 3). A Casoni test was negative. The Mantoux test at 1 : 1000 was positive.

At this stage it was important to decide what the tumour was and whether it might be amenable to surgery. The following possibilities were considered:

1. A mass arising from the heart (primary or secondary tumour, aneurysm containing clot);
2. A pericardial mass (localized pericardial effusion or haematoma, in view of the previous history of scurvy);
3. An extracardiac mass (hilar or mediastinal).

Physical examination and X-rays revealed no obvious primary neoplasm in the lungs, gastro-intestinal tract and the genito-urinary tract. The diagnosis of primary auricular neoplasm seemed possible, particularly in the presence of paroxysmal auricular tachycardia, but there was no paroxysmal dyspnoea or pulmonary congestion—signs which have been reported in some of these cases.[2]

The most likely possibilities seemed to be an extracardiac mass or localized tuberculous pericarditis, a condition we had previously encountered in another patient. As some of these tumours might be amenable to surgery, the patient was submitted to thoracoscopy. This procedure showed the medial surface of the left lung to be adherent to the pericardium along its whole anterior edge and no conclusion could be arrived at about the nature of the mass.

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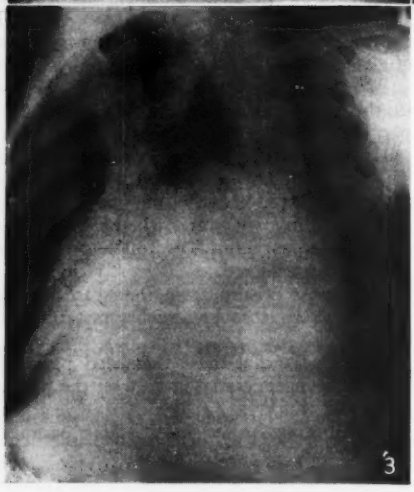

Fig. 1. X-ray on admission showing generalized cardiac enlargement and minimal pulmonary congestion.
Fig. 2. X-ray showing a mass at the left cardiac border.
Fig. 3. Oblique view showing situation of the mass.

Thoracotomy was performed a week later. A large collection of clear yellow fluid was found encapsulated between the lung and the heart, the space extending from the aorta to the diaphragm and from the hilum of the lung anteriorly. The inner surface was lined by a thin layer of organizing fibrin, easily stripped from the surfaces of the lung and pericardium. A number of glands could be felt in the hilum and in the mediastinum, but none was large or softened, or had broken through the pleura. The adherent edge of the lung was separated from the pericardium and the fluid aspirated. There was no excess pericardial fluid. The chest was closed without drainage. Histology of the excised tissue revealed only non-specific chronic inflammatory change.

Progress. Within 48 hours the patient was remarkably improved. He became less dyspnoeic and his venous congestion subsided. Within 2 weeks he lost his oedema, his heart became smaller (Fig. 4) and his liver, enlarged 2 finger breadths, was the only evidence of his original venous engorgement. He has continued to improve and when last seen was going about his ordinary duties.

Comment. There is no doubt that the locu-

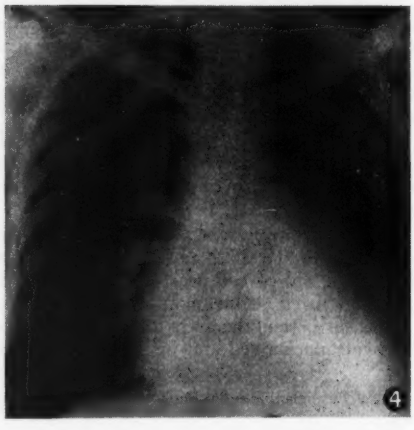

Fig. 4. 3 weeks after operation.

lated mass of fluid caused the heart failure in this patient. We knew that his heart had been normal 2 years before and he recovered rapidly from his heart failure after the fluid was released. Since tuberculosis is so common in Africans the chances are that the effusion was tuberculous, although microscopy did not confirm this.

Examples of heart failure due to extrinsic pressure by tumour or fluid are rare and it is interesting to speculate on the mechanism in this case. It was not due to compression of the great veins, since his neck veins pulsated freely and a hepato-jugular reflux could be elicited. It is unlikely that it was due to pressure on the left ventricle or the left auricle, as we would have expected more signs of left auricular or left ventricular failure, viz. paroxysmal dyspnoea and pulmonary congestion. The presenting clinical picture, a hypodynamic circulation and pulsus paradoxus, resembled that of pericardial effusion or constrictive pericarditis, and suggested that the mechanism of failure was probably cardiac tamponade.

The post-operative course was dramatic. Unlike patients suffering from chronic tuberculous pericarditis, whose signs of congestive heart failure clear slowly after pericardiectomy, this patient lost virtually all his signs within a fortnight. Although the basic disturbance in both conditions is probably similar, viz. interference with diastolic relaxation of the heart, the rapidity of the response in this case is presumably explicable by the comparatively short duration of the constricting factor.

OPSOMMING

Die skrywers doen verslag oor 'n geval van hartvervlamming ten gevolge van 'n sakkies-agtige massa vloeistof, waarskynlik tuberkuleus van oorsprong, wat tussen die long en die hart ingekapsel was.

Na opsuiging van die vloeistof (in 'n ruimte wat vanaf die grootliggaamslagaar na die middelrif en van die hilum van die long na sy voorste grens gestrek het), het die toestand van die pasiënt vinnig en op 'n merkwaardige wyse verbeter.

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PREPARATE EN TOESTELLE

PARENOGEN: MENSLIKE FIBRINOGEEN

INDIKASIES VIR PARENOGEN-TERAPIE

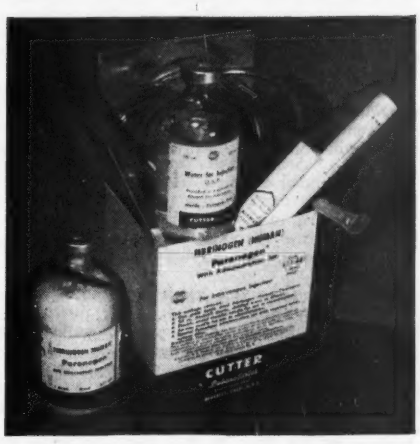
(*a*) *Ontydige Loslating van die Placenta met Afibrinogeenemie*: Daar word erken dat afibrinogeenemie wat tydens swangerskap voorkom en gekompliseer word deur ernstige gevalle van loslating van die placenta, reeds 'n aansienlike aantal sterfgevalle veroorsaak het. In sulke toestande is vervangingsterapie met fibrinogeen en bloed van die allergrootste belang.

Dit is moeilik om 'n ernstige geval vóór bevalling te herken. Daar word derhalwe aan die hand gedoen dat, in alle gevalle van ontydige loslating, klontvormingstudies, insluitende 'n ondersoek na die plasma-fibrinogeen-peil, onderneem moet word. Oor die algemeen is 'n plasma-fibrinogeen-peil van minder as 50 mg.% kritiek, en fibrinogeen-(*Parenogen*-) terapie moet dan onmiddellik ingestel word.

(*b*) *Uitgebreide Chirurgiese Prosedures*: Akute afibrinogeenemie is ook gerapporteer in gevalle wat geassosieer was met drastiese borskaschirurgie, alvleesklierchirurgie en ander chirurgiese en traumatiese toestande.

Wanneer klontvormingsdefekte hul verskyning in die loop van hierdie prosedures maak, behoort die laboratoriumstudies vir die vasstelling van die aard van die klontvormingsdefekte ook 'n vasstelling van die plasma-fibrinogeen-peil in te sluit. Waar 'n fibrinogeen-peil van minder as 100 mg.% aangetref word, moet daar ernstige oorweging aan die toediening van *Parenogen* verleen word.

(*c*) *Aangebore of Verworwe Chroniese Afibrinogeenemie*: Aangebore afibrinogeenemie is 'n sonderlinge siekte voortspruitende uit 'n versteuring van die proteïenmetabolisme wat geopenbaar word deur sy ingrypende effek op die bloedstollingsmeganisme.



In hierdie sonderlinge gevalle kan *Parenogen* bes moontlik aangedui word vir die instandhouding van die plasma-fibrinogeen-peil wat skynbaar

ernstige bloeding voorkom. Oor die algemeen sal hierdie pasiënte 'n verbasende lae fibrinogeen-peil verdra sonder bloeding.

Parenogen is die enigste kommersieel voorbereide menslike fibrinogeen wat tans beskikbaar is. Iedere flessie word verkry van normale menslike plasma en is bakteriologies steriel en nie-koorsverwekkend, en is onderwerp aan ultravioletbestraling.

Iedere pakkie bevat 1.0 g. stolbare fibrinogeen wat met behulp van 50 k.s. steriele, gedistilleerde water gerekonstitueer moet word. Die gerekonstitueerde stof moet binne 'n uur na voorbereiding gebruik word.

Enigste Suid-Afrikaanse Verspreiders: Protea Pharmaceuticals Limited, Posbus 7793, Johannesburg.

PREPARATIONS AND APPLIANCES

PARENOGEN: HUMAN FIBRINOGEN

INDICATIONS FOR PARENOGEN THERAPY

(*a*) *Premature Separation of the Placenta with Afibrinogenaemia*: Afibrinogenaemia occurring during pregnancies complicated by severe cases of abruptio placentae has been recognized as the cause of an appreciable number of deaths. In this condition replacement therapy with fibrinogen and blood is of primary importance.

It is difficult to recognize a severe case before delivery. Therefore it is suggested that in all cases of premature separation, coagulation studies, including plasma fibrinogen level, be done. In general, a plasma fibrinogen level of less than 50 mg.% is critical, and fibrinogen (*Parenogen*) therapy should be instituted immediately.

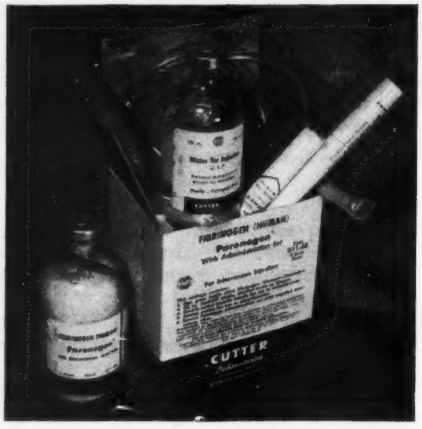
(*b*) *Extensive Surgical Procedures*: Acute afibrinogenaemia has also been reported in instances associated with drastic thoracic surgery, pancreatic surgery and other surgical and traumatic conditions.

When coagulation defects appear in the course of these procedures, laboratory studies to determine the nature of the coagulation defect should include determinations of plasma fibrinogen levels. When levels of fibrinogen below 100 mg.% are found, the administration of *Parenogen* should be seriously considered.

(*c*) *Congenital or Acquired Chronic Afibrinogenaemia*: Congenital afibrinogenaemia is a rare disease involving a disturbance of protein metabolism manifested by its profound effect on the blood clotting mechanism.

In these rare cases *Parenogen* may be indicated to maintain a plasma fibrinogen level that appears to prevent severe haemorrhage. Generally these patients will tolerate a surprisingly low fibrinogen level without haemorrhage.

Parenogen is the only commercially prepared human fibrinogen now available. Each vial is derived from normal human plasma and is bacteriologically sterile, non-pyrogenic and has been subjected to ultraviolet irradiation.



Each package contains 1.0 g. of clottable fibrinogen which must be reconstituted with 50 c.c. of sterile distilled water. The reconstituted material must be used within one hour of preparation.

Sole South African Distributors: Protea Pharmaceuticals Limited, P.O. Box 7793, Johannesburg.

NOTES AND NEWS · BERIGTE

Dr. Thomas J. Dry, M.A., M.B., Ch.B. (University of Cape Town), M.S. in Medicine (University of Minnesota), Diplomate of the American Board of Internal Medicine, Fellow of the American College of Physicians and formerly Professor of Medicine, Mayo Foundation, has returned to South Africa and resumed practice as a physician at 314, Netherlands Bank Building, 85 St. George's Street, Cape Town.

During World War II, Dr. Dry was Chief of Medical Service in various hospitals, with the rank of Lieutenant-Colonel on discharge.

Dr. Dry, a distinguished graduate of the University of Cape Town, is the author of several important publications which include *A Manual of Cardiology* (2nd ed.), *An Atlas of Congenital Anomalies of the Heart and Great Vessels, Treatment of Heart Disease in General Medicine* and *A History of the Heart and Circulation* (with F. A. Willius).

AFIBRINOGENAEMIA AND FIBRINOGEN

Acute, total afibrinogenemia was observed a few hours after the completion of an apparently uneventful elective cesarean section. The ensuing hemorrhage did not respond to multiple bank-blood

transfusions but ceased immediately after the administration of human fibrinogen. It is assumed that thromboplastic proteins may have entered the venous circulation during surgery, but predisposing factors for such an event are not known.

(*From* Leary, J. J. (1956): Obstet. Gynec., **7**, 150).

SCIENTIFIC EXHIBITION: 1957 DURBAN MEDICAL CONGRESS

A Scientific Exhibition will be one of the main features of the 1957 Medical Congress at Durban, and this will offer a unique opportunity for the demonstration of scientific work being carried out in the Union, not only by officially sponsored research units, but also by individual doctors who will, it is hoped, play a big part in the Exhibition. Apart from pure medical research, the scope of the Exhibition may include anthropology and genetics, psychology and industrial aptitude testing, public health and sanitation, medical aspects of atomic energy, nutrition, food technology and quality control, therapeutic substances (production and control), veterinary science and the zoonoses, hospital planning and medical services organization, blood transfusion, the history of medicine and its instruments and tribal medicine and customs.

The Exhibition will be quite separate from the Trades and Doctors' Hobbies Exhibition.

One part of the Exhibition will be a cinematograph theatre showing a daily programme of medical and scientific films and film strips or transparencies.

Will all those who wish to take part in this Exhibition, please inform the Scientific Exhibition Committee (*Chairman*: Dr. J. C. Thomas; *Honorary Secretaries*: Mr. G. Stafford Mayer and Dr. E. E. Rosenberg), 112 Medical Centre, Field Street, Durban, *as soon as possible*, stating the nature of their exhibit, the approximate linear or square footage of display space, whether power, water, drainage or gas will be required, and the approximate showing time for films or slides.

THE SOUTH AFRICAN SOCIETY OF SPECIALISTS IN PHYSICAL MEDICINE

At the International Congress of Physical Medicine held in Copenhagen on 19 August 1956, the South African Society was elected to full membership of the International Federation of Physical Medicine.

BOOK REVIEW

TOXICITY OF PESTICIDES

Toxic Hazards of Pesticides to Man: Report of a Study Group. World Health Organization: Technical Report Series, 1956, No. 114, pp. 51, 3s. 6d. Van Schaik's Bookstore (Pty.) Ltd., P.O. Box 724, Pretoria.

The widespread and ever growing use of pesticides to control vectors of disease and to safeguard crops has brought in its wake some special problems. Foremost among these is the question whether the wholesale application of these products is likely to have an adverse effect on human health.

The World Health Organization first took a serious interest in this question in 1952, when it appointed a special consultant (Dr. J. M. Barnes) to study the whole problem. In his *Report*, published in 1953 as No. 16 in the *WHO Monograph Series*, Dr. Barnes concluded that pesticides, if properly used, did not represent any immediate or serious threat to human health. Nevertheless, he went on to say that a continuing watch should be kept on the situation, since new uses and the development of new materials might at any time introduce potentially dangerous factors, and advocated that the subject should be studied further on as wide a basis as possible. As a result of Dr. Barnes's recommendations, a Study Group, composed of experts with specialized knowledge of the toxicity of pesticides on the one hand, and of their practical use in agriculture and public health work on the other, was convened by WHO in June 1956.

In its introduction, the Group's *Report* points out that the evolution of resistant strains of insects may make it necessary in the near future to use new types of insecticides in malaria control, and states that, in view of this, the Group 'considered in some detail the recommendations that might be made to enable more toxic insecticides of all kinds to be used safely in public health work'. Then, after defining the term 'pesticides', the *Report* proceeds to discuss the toxic properties of these substances, stressing the importance of carrying out field investigations as well as laboratory experiments in this connexion.

This is followed by a review of the incidence and nature of poisoning, in which the clinical signs of poisoning are described and laboratory methods for detecting the presence of pesticides in the body are discussed.

Attention is then turned to the more immediate and practical problem of the measures to be taken to protect operators handling pesticides, with emphasis on the importance of distributing information on hazards to all workers concerned with pesticides. Both the general precautions to be observed by all spray operators and the special precautions necessary when dealing with the more toxic materials, such as dieldrin and the organophosphorus compounds, and when carrying out aerial spraying operations, are described.

Next, the *Report* deals at some length with the question of the hazards arising from the deliberate or accidental addition of pesticides to drinking water or food supplies, and more briefly with the effects on domestic animals and fish of the extensive use of pesticides.

In conclusion, the role of governmental regulation in the prevention of hazards during the manufacture, handling and application of pesticides and the control of pesticide residues in food is considered.

Annexed to the report are (i) a summary of the results of a questionnaire which was sent to a number of laboratories engaged in research on the vertebrate toxicology of pesticides to find out how many were employed on such work and what types of investigation were being carried out; (ii) a brief account of a study of the degree of exposure of workers to insecticides; and (iii) recommendations for the design and use of respirators.

CORRESPONDENCE

NOVOBIOCIN

To the Editor: I have read with considerable interest the letter by Dr. M. M. Zion appearing in the 27 October issue of this Journal. The suggestions made in his letter are questionable.

He states in opening: 'The Editorial on *Novobiocin* in your issue of 15 August 1956 mentions that, with the use of this antibiotic, no monilial super-infection has been reported. This prompts me to report briefly the following case, in which, while there is no proof that novobiocin was in fact responsible, much suspicion rests on this drug for having precipitated monilial super-infection of the bowel.'

Yet it is noteworthy that he concludes with these remarks: 'The novobiocin thus seems to be the most likely drug responsible if, in fact, a drug is to be incriminated.'

It should be noted that:

1. The original condition of a red and raw palate treated empirically with penicillin was not diagnosed microscopically.
2. The second condition of a recurring sore throat accompanied by diarrhoea, pyrexia, enlarged tonsils and sores on the nose and lips was not diagnosed microscopically and the patient was empirically treated with novobiocin.
3. The third condition of a recurring diarrhoea (but now with blood and mucus) was not diagnosed microscopically even though treated with chloramphenicol for 24 hours.
4. Only after this, and then for the first time, were two specimens examined and found to contain *Candida albicans* and *P. morgani*; a third and last specimen, with no intervening treatment, was found to be free from pathogenic bacteria and fungi!
5. The patient then left town and there was no opportunity for further investigation.

There is nothing in this correspondence to indicate that a microscopic diagnosis was made to determine the presence or absence of monilia *before* the use of penicillin, novobiocin or chloramphenicol.

On current, reasonably extensive knowledge from *controlled* clinical investigation, there is little probability that novobiocin can produce such effects; and no facts have been given that would contradict present knowledge of the relationship between novobiocin and monilia.

New and personal reports are desirable but only if they are based on scientifically controlled data.

Civis Candidus.

Johannesburg.

OEDEMA AFTER RAUWOLFIA THERAPY

To the Editor: In the Correspondence Columns of your issue of 15 September 1956, Mr. R. E. Holmes stated on p. 500 that only reserpine had been reported as causing oedema, during Rauwolfia therapy.

The published evidence does not support this statement. Perera[1] described 5 cases of oedema following Rauwolfia preparations (i.e. 3 following reserpine and 2 following whole root Rauwolfia preparations). McGregor and Segal[2] observed 2 cases of oedema following treatment with Rauwolfia preparations. (One case followed reserpine, the other a crude root preparation).

The question of oedema following Rauwolfia preparations might be better summed up as follows. Oedema after Rauwolfia preparations is rare, but it is clear from the foregoing references that it can follow treatment with reserpine, with whole root preparations, as well as with mixed alkaloids. If more cases have been reported following reserpine therapy, the much greater frequency of the use of reserpine, as a form of Rauwolfia therapy, would readily explain more frequent reports. It has not been proved, nor is it at all likely, that fluid retention is due to heart failure provoked by reserpine. Renal damage caused by reserpine is also out of the question.

Foote[3] described 2 cases of oedema of the face and the legs following reserpine therapy, although no weakness of the heart or renal disorder was present. Foote suggests that the oedema was possibly due to the drug's influence on higher cerebral centres. Perera[1] refuses to believe that the fluid retention is of renal origin and is, in fact, unable to offer any satisfactory explanation for its appearance.

Ferguson,[4] like Foote, thinks that reserpine may cause fluid retention by influencing central mechanisms, and he stresses that the cardiac muscle is not necessarily impaired.

Maurel *et al.*,[5] in reporting oedema after Rauwolfia therapy, mention the localization of the oedema in the face and lower extremities, which may indicate that the condition was not of cardiac origin. These authors also point out that the symptoms were benign and rapidly reversible.

The encouraging results which have already been obtained with reserpine in certain types of heart disease[6-8] are in themselves sufficient to warrant the conclusion that the fluid retention which sometimes occurs in the course of reserpine therapy, is not of cardiac origin.

The most plausible explanation is that the oedema is brought about by some influence on water and electrolyte balance of endocrine origin. This, however, is only an assumption, since even to-day the aetiology of oedema is something of an enigma.

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